

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

NIPPON SHINYAKU CO., LTD.,
Plaintiff,

v.

SAREPTA THERAPEUTICS, INC.,
Defendant.

SAREPTA THERAPEUTICS, INC. and THE
UNIVERSITY OF WESTERN AUSTRALIA,
Defendant/Counter-Plaintiffs,

v.

NIPPON SHINYAKU CO., LTD. and NS
PHARMA, INC.,
Plaintiff/Counter-Defendants.

)
)
) C.A. No. 21-1015 (GBW)

)
) **DEMAND FOR JURY TRIAL**
)

) [REDACTED]

) [REDACTED]
)

**PLAINTIFF'S CONCISE STATEMENT OF FACTS IN SUPPORT OF ITS MOTION
FOR PARTIAL SUMMARY JUDGMENT NO. 1 REGARDING
INVALIDITY OF THE UWA PATENTS**

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Dated: December 11, 2023

UWA PATENTS

1. The UWA Patents each claim priority to PCT/AU2005/000943, filed June 28, 2005. The UWA Patents share a materially identical specification. The shared specification states that “[t]he oligonucleotide and the DNA or RNA are complementary to each other when a sufficient number of corresponding positions in each molecule are occupied by nucleotides which can hydrogen bond with each other.” D.I. 2-9, Ex. I (’851 Patent) at 25:18-21. The specification explains:

Thus, “specifically hybridisable” and “complementary” are terms which are used to indicate a sufficient degree of complementarity or precise pairing such that stable and specific binding occurs between the oligonucleotide and the DNA or RNA target. It is understood in the art that the sequence of an antisense molecule need not be 100% complementary to that of its target sequence to be specifically hybridisable.

Id. at 25:21-28. The specification states that the “[o]ligonucleotides may also include nucleobase (often referred to in the art simply as ‘base’) modifications or substitutions.” *Id.* at 27:35-37. The specification states that “[a]nother modification of the oligonucleotides of the invention involves chemically linking to the oligonucleotide one or more moieties or conjugates that enhance the activity, cellular distribution or cellular uptake of the oligonucleotide.” *Id.* at 27:47-51.

2. The specification describes experimental work for 219 AOs targeted to various exons of the human dystrophin pre-mRNA. *Id.* at 4:44-49, tbl. 1A; *see also id.* at 4:56-61, tbl. 1C. The specification describes a single AO that induces exon 53 skipping and includes the claimed “at least 12 consecutive bases of” SEQ ID NO. 195—SEQ ID NO. 195 itself. D.I. 2-9, Ex. I (’851 Patent) at tbl. 39; Ex. 13 (Dowdy Dep.) at 188:10-15. SEQ ID NO. 195 targets position +23+47. SEQ ID NO. 195 is a 2’-O-Me AO with uracil bases. D.I. 2-9, Ex. I (’851 Patent) at Table 1A, Table 39; Ex. 2 (Dowdy Rebuttal) ¶ 109. SEQ ID NO. 195 induced “very faint skipping to 50 nM.”

D.I. 2-9, Ex. I ('851 Patent) at Table 39. The UWA Patents do not disclose an AO targeting positions +36+60 or an AO targeting positions+36+56.

3. The specification *does not* (1) disclose any test results for a PMO; (2) disclose any test results for an AO with thymine bases; (3) disclose any test results for an AO that includes the claimed “at least 12 consecutive bases of” SEQ ID NO. 195 and is 20, 21, 22, 23, 24, 26, 27, 28, 29, 30, or 31 bases in length; (4) disclose any examples of an AO that induces exon 53 skipping that is 20, 22, 23, 26, 28, 29 or 30 bases in length; (5) disclose any test results for an AO with any number of mismatches, insertions, or deletions versus the human exon 53 pre-mRNA (i.e., is not 100% complementary); (6) disclose any test results for an AO with nucleobase chemical modifications; (7) disclose any test results for an AO linked to a chemical moiety; (8) disclose the term “hot spot,” “hotpot” or “hot-spot”; (9) state that the region delineated by positions +23+69 in the human exon 53 pre-mRNA is a region amenable to exon skipping.

4. At his November 8, 2023 deposition, Dr. Dowdy testified that [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]. Specifically, Dr. Dowdy testified:

[REDACTED]

[REDACTED]

[REDACTED]

THE SCOPE OF THE UWA PATENTS CLAIMS IS VAST

5. [REDACTED]

[REDACTED]

[REDACTED] Ex. 5 (Hastings Opening) ¶ 48. Using this formula, [REDACTED]
[REDACTED]
[REDACTED] *Id.* At his November 8, 2023 deposition, Dr. Dowdy agreed [REDACTED]
[REDACTED]
[REDACTED]” Ex. 13 (Dowdy Dep.) at 198:13-20. Dr. Dowdy testified that
aside [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

6. According to Dr. Dowdy, [REDACTED]
[REDACTED] Dr. Dowdy
opines that “[REDACTED]
[REDACTED] Ex. 2 (Dowdy Rebuttal) ¶ 57. With this assumption,
[REDACTED]
[REDACTED] *Id.* ¶ 58.

7. At his November 8, 2023 deposition, Dr. Dowdy [REDACTED] “[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]” Ex. 13 (Dowdy Dep.) at 16:24–17:6. Dr. Dowdy testified that [REDACTED]

[REDACTED]

[REDACTED] Ex. 13 (Dowdy Dep.) at 15:14–17:22; *see also id.* at 203:2–6. With this assumption, [REDACTED]

[REDACTED]

8. Dr. Dowdy also acknowledged that [REDACTED]

[REDACTED]

[REDACTED]” *Id.* at 36:3-17. In applying the Court’s construction, Dr. Hastings [REDACTED]. Ex. 5 (Hastings Opening) ¶ 48.

9. Dr. Dowdy’s calculation considers [REDACTED]

[REDACTED]” Ex. 7 (Hastings Reply) ¶ 14, n.2; *see also* Ex. 2 (Dowdy Rebuttal) ¶ 57, n.6 ([REDACTED]). Thus, the “[REDACTED]” Ex. 7 (Hastings Reply) ¶ 14.

EXON SKIPPING WAS UNPREDICTABLE AT THE TIME OF THE INVENTION AND REMAINS UNPREDICTABLE TODAY

10. As Sarepta argued during the prosecution of the ’851 Patent, “[t]here was a significant level of unpredictability . . . at the time of the invention.” Ex. 29 (SRPT-VYDS-0002984) at 4784. To make this argument, Sarepta relied on publications from 2002 and 2003 to argue that “interfering with exon selection for inclusion before splicing is ‘a process that is not yet well understood’” and “that significant experimentation is required to arrive at specific oligonucleotides” because there was “no insight into the actual position of the targeted sequence within the completely folded RNA structure.” *Id.* at 4790-4792. Sarepta also described “examples

of unpredictability [] reported ... at or near the date of Applicants' invention." *Id.* at 4792-4793. As Sarepta explained, this unpredictability applied "even in situations where the antisense oligonucleotides are very similar to each other in terms of nucleotide sequence, and other variables concerning the chemical backbone are fixed." *Id.* at 4793.

11. Sarepta further explained how the "recognition of the lack of predictability in the field of exon skipping continued beyond 2005." *Id.* at 4793-4794. Sarepta pointed to a 2007 publication explaining that "there are still no clear rules to guide investigators in their design" and a 2009 publication noting that "in general a trial and error procedure is still involved to identify potent AONs." *Id.* Sarepta also relied on a 2011 publication as evidence that "selecting specific antisense oligonucleotide sequences to induce effective dystrophin exon skipping remains an unpredictable exercise." *Id.* at 4794-4795.

12. Sarepta made similar arguments during an interference proceeding against Leiden University Medical Centre in Interference No. 106,007 ("Interference '007"). During that proceeding, Sarepta told the Patent Office that "[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]" Ex. 23 (UWA Motion 1) at 4. Sarepta also told the Patent Office that "[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]" *Id.*

13. Sarepta stated:

[REDACTED]

[REDACTED]

Id. at 1 (emphasis added).

14. Dr. Dowdy [REDACTED]

[REDACTED]

[REDACTED]. Dr. Dowdy testified that “[REDACTED]” Ex. 13 (Dowdy Dep.) at

44:4-15. Dr. Dowdy also testified that t [REDACTED]

[REDACTED]. *Id.* at 44:20-22 [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED].

15. As Sarepta argued during Interference ’007, the need to test each and every potential AO to determine whether an AO falls within the scope of the claims (*i.e.*, whether it induces exon 53 skipping) is reflected in the specification of the UWA Patents. Ex. 24 (UWA Reply 1) at 9 (“[REDACTED]

[REDACTED]

[REDACTED].”).

CERTIFICATE OF SERVICE

The undersigned certifies that on December 11, 2023, a copy of the foregoing, which was filed under seal, was served via electronic mail on the following counsel of record:

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